Attorney's Docket No.: 0.25-001001 / 50731US006

Applicant: Thomas H. Barrows et Serial No.: 09/185 732

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integer from 2-10, and R is a polymer or copolymer having 1-10 monomeric fragments selected from the group consisting of lactide, glycolide, trimethylene carbonate, caprolactone and p-dioxanone; [and]

wherein -G is a leaving group selected from the group consisting of succinimidyl, maleimidyl, phthalimidyl, imidazolyl, nitrophenyl, [or] and tresyl[,]; and

wherein a combination of the first and second mixtures is initially liquid and then cures on the surface of tissue to give a flexible, substantive matrix which bonds to the tissue and has a burst strength greater than about 10 mmHg.

15. (Amended) The adhesive [mixture] <u>composition</u> of claim 1 wherein -LM- is a diester diradical of the formula[,] -C(O)-(CH<sub>2</sub>)<sub>c</sub>-C(O)- where c is an integer from 2-10 and where the aliphatic portion of the diradical may be saturated or unsaturated.

17. (Amended) A method of making a tissue adhesive consisting of the step of forming a mixture of

- i) a first aqueous mixture of about 20-60 wt/vol % serum albumin in about 0.01-0.25 molar buffer at a pH in a range of about 8.0-11.0,
- ii) a second aqueous mixture of about 50-800 mg/ml of a crosslinking agent having a molecular weight in a range of about 1,000-15,000, wherein the crosslinking agent is of the formula

G-LM-PEG-LM-G

wherein -PEG- is a diradical fragment represented by the formula

-O-(CH<sub>2</sub>-CH<sub>2</sub>-O-)<sub>a</sub>-

where a is an integer from 20-300;

wherein -LM- is a diradical fragment selected from the group consisting of a carbonate diradical of the formula[,] -C(O)-, a monoester diradical of the formula[,] -(CH<sub>2</sub>)<sub>b</sub>C(O)- where b is an integer from 1-5, a diester diradical of the formula[,] -C(O)-(CH<sub>2</sub>)<sub>c</sub>-C(O)- where c is an integer from 2-10 and where the aliphatic portion of the diradical may be saturated or unsaturated, a dicarbonate diradical of the formula -C(O)-O-(CH<sub>2</sub>)<sub>d</sub>-O-C(O)- where d is an integer from 2-10, and an oligomeric diradical represented by the formulas -R-C(O)-,

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-R-C(O)-(CH<sub>2</sub>)<sub>c</sub>-C(O)-, or -R-C(O)-O-(CH<sub>2</sub>)<sub>d</sub>-O-C(O)- where c is an integer from 2-10, d is an integer from 2-10, and R is a polymer or copolymer having 1-10 monomeric fragments selected from the group consisting of lactide, glycolide, trimethylene carbonate, caprolactone and p-dioxanone; [and]

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wherein -G is a leaving group selected from the group consisting of succinimidyl, maleimidyl, phthalimidyl, imidazolyl, nitrophenyl, [or] and tresyl[,]; and

wherein a combination of the first and second mixtures is initially liquid and then cures on the surface of tissue to give a flexible, substantive matrix which bonds to the tissue and has a burst strength greater than about 10 mmHg.

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